



## SEQUENCE LISTING

#7

<110> Duke University  
Lin, Haifan

<120> PURIFIED AND ISOLATED piwi FAMILY GENES AND GENE  
PRODUCTS AND THERAPEUTIC AND SCREENING METHODS USING SAME

<130> Attorney Docket No. 180-104/2

<140> 09/873,737

<141> 2001-06-04

<150> PCT/US99/28764

<151> 1999-12-03

<150> 60/110,901

<151> 1998-12-04

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<170> PatentIn Ver. 2.1

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Met Ala Asp Asp Gln Gly Arg Gly Arg Arg  
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Arg Pro Xaa Asn Glu Asp Asp Ser Ser Thr Ser Arg Gly Ser Gly Asp  
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Gly Pro Arg Val Lys Val Phe Arg Gly Ser Ser Ser Gly Asp Pro Arg  
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| Ala Asp Pro Arg Ile Glu Ala Ser Arg Glu Arg Arg Ala Leu Glu Glu |     |
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| gct ccc agg cgt gaa ggt ggc ccg cca gag cga aag ccg tgg ggt gac | 305 |
| Ala Pro Arg Arg Glu Gly Gly Pro Pro Glu Arg Lys Pro Trp Gly Asp |     |
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| caa tat gat tac ctg aat acc cgt ccg gtt gag ctg gta tcc aag aag | 353 |
| Gln Tyr Asp Tyr Leu Asn Thr Arg Pro Val Glu Leu Val Ser Lys Lys |     |
| 75 80 85 90   |     |
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| Gly Thr Asp Gly Val Pro Val Met Leu Gln Thr Asn Phe Phe Arg Xaa |     |
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| aaa acc aag ccg gaa tgg cgg atc gtt cat tat cac gtg gag ttt gtg | 449 |
| Lys Thr Lys Pro Glu Trp Arg Ile Val His Tyr His Val Glu Phe Val |     |
| 110 115 120   |     |
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| Pro Thr Ile Glu Asn Pro Arg Val Arg Met Gly Val Leu Ser Asn His |     |
| 125 130 135   |     |
| gct aac ctt ctg gga tca ggc tat cta ttc gac gga ctg caa ctg ttc | 545 |
| Ala Asn Leu Leu Gly Ser Gly Tyr Leu Phe Asp Gly Leu Gln Leu Phe |     |
| 140 145 150   |     |
| acc acc agg aaa ttc gag cag gaa atc acg gtg ctc agc gga aag tcg | 593 |
| Thr Thr Arg Lys Phe Glu Gln Glu Ile Thr Val Leu Ser Gly Lys Ser |     |
| 155 160 165 170   |     |
| aag ctg gac att gaa tac aag ata tcc ata aag ttc gtt gga ttc ata | 641 |
| Lys Leu Asp Ile Glu Tyr Lys Ile Ser Ile Lys Phe Val Gly Phe Ile |     |
| 175 180 185   |     |
| tcg tgt gct gag ccc cgc ttt ttg caa gtc tta aat cta ata ttg cgc | 689 |
| Ser Cys Ala Glu Pro Arg Phe Leu Gln Val Leu Asn Leu Ile Leu Arg |     |
| 190 195 200   |     |
| cgc tcg atg aag ggc cta aat ttg gaa tta gtt ggc cgt aat ctc ttt | 737 |
| Arg Ser Met Lys Gly Leu Asn Leu Glu Leu Val Gly Arg Asn Leu Phe |     |
| 205 210 215   |     |
| gat ccc cga gct aag atc gaa ata agg gag ttc aaa atg gag cta tgg | 785 |
| Asp Pro Arg Ala Lys Ile Glu Ile Arg Glu Phe Lys Met Glu Leu Trp |     |
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| ccg ggc tat gag aca tcg att cgt cag cac gaa aaa gat att tta ttg | 833 |
| Pro Gly Tyr Glu Thr Ser Ile Arg Gln His Glu Lys Asp Ile Leu Leu |     |
| 235 240 245 250   |     |
| ggc acc gaa ata act cac aaa gtt atg cgc acc gag acg atc tac gac | 881 |
| Gly Thr Glu Ile Thr His Lys Val Met Arg Thr Glu Thr Ile Tyr Asp |     |
| 255 260 265   |     |
| ata atg cga cgt tgc tca cac aat ccg gct cgt cat cag gac gaa gta | 929 |
| Ile Met Arg Arg Cys Ser His Asn Pro Ala Arg His Gln Asp Glu Val |     |
| 270 275 280   |     |

|                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |                   |      |
|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|------|
| cgg<br>Arg        | gta<br>Val        | aat<br>Asn<br>285 | gtt<br>Val        | ttg<br>Leu        | gac<br>Asp        | ttg<br>Leu        | att<br>Ile<br>290 | gtc<br>Val        | ctt<br>Leu        | acg<br>Thr        | gat<br>Asp        | tac<br>Tyr<br>295 | aat<br>Asn        | aac<br>Asn        | aga<br>Arg        | 977  |
| act<br>Thr        | tat<br>Tyr<br>300 | cgt<br>Arg        | atc<br>Ile        | aat<br>Asn        | gat<br>Asp        | gtc<br>Val<br>305 | gac<br>Asp        | ttt<br>Phe        | gga<br>Gly        | caa<br>Gln        | act<br>Thr<br>310 | ccg<br>Pro        | aaa<br>Lys        | tca<br>Ser        | aca<br>Thr        | 1025 |
| ttc<br>Phe<br>315 | agt<br>Ser        | tgc<br>Cys        | aag<br>Lys        | ggg<br>Gly        | aga<br>Arg<br>320 | gat<br>Asp        | atc<br>Ile        | agt<br>Ser        | ttc<br>Phe        | gtg<br>Val<br>325 | gaa<br>Glu        | tac<br>Tyr        | tat<br>Tyr        | ctc<br>Leu        | act<br>Thr<br>330 | 1073 |
| aaa<br>Lys        | tat<br>Tyr        | aat<br>Asn        | ata<br>Ile        | cgc<br>Arg<br>335 | att<br>Ile        | cgc<br>Arg        | gac<br>Asp        | cac<br>His        | aat<br>Asn<br>340 | cag<br>Gln        | ccg<br>Pro        | ctg<br>Leu        | ctg<br>Leu        | att<br>Ile<br>345 | tcc<br>Ser        | 1121 |
| aaa<br>Lys        | aat<br>Asn        | agg<br>Arg        | gac<br>Asp<br>350 | aag<br>Lys        | gct<br>Ala        | cta<br>Leu        | aaa<br>Lys        | act<br>Thr<br>355 | aac<br>Asn        | gct<br>Ala        | agc<br>Ser        | gaa<br>Glu        | tta<br>Leu<br>360 | gtg<br>Val        | gta<br>Val        | 1169 |
| cta<br>Leu        | att<br>Ile        | cct<br>Pro<br>365 | gag<br>Glu        | ctc<br>Leu        | tgc<br>Cys        | cga<br>Arg        | gtg<br>Val<br>370 | act<br>Thr        | ggg<br>Gly        | ctc<br>Leu        | aat<br>Asn        | gcc<br>Ala<br>375 | gag<br>Glu        | atg<br>Met        | cgc<br>Arg        | 1217 |
| tca<br>Ser        | aac<br>Asn<br>380 | ttt<br>Phe        | cag<br>Gln        | ctt<br>Leu        | atg<br>Met        | cgt<br>Arg<br>385 | gcc<br>Ala        | atg<br>Met        | agc<br>Ser        | agt<br>Ser        | tat<br>Tyr<br>390 | acg<br>Thr        | cga<br>Arg        | atg<br>Met        | aac<br>Asn        | 1265 |
| ccc<br>Pro<br>395 | aaa<br>Lys        | caa<br>Gln        | cgc<br>Arg        | act<br>Thr        | gat<br>Asp<br>400 | cga<br>Arg        | ttg<br>Leu        | cgc<br>Arg        | gct<br>Ala        | ttt<br>Phe<br>405 | aac<br>Asn        | cac<br>His        | cgt<br>Arg        | tta<br>Leu        | caa<br>Gln<br>410 | 1313 |
| aac<br>Asn        | act<br>Thr        | cca<br>Pro        | gaa<br>Glu        | agt<br>Ser<br>415 | gtg<br>Val        | aag<br>Lys        | gtc<br>Val        | ttg<br>Leu        | aga<br>Arg<br>420 | gac<br>Asp        | tgg<br>Trp        | aac<br>Asn        | atg<br>Met        | gaa<br>Glu<br>425 | ctg<br>Leu        | 1361 |
| gac<br>Asp        | aag<br>Lys        | aac<br>Asn        | gtc<br>Val<br>430 | aca<br>Thr        | gaa<br>Glu        | gta<br>Val        | caa<br>Gln        | ggc<br>Gly<br>435 | cgg<br>Arg        | ata<br>Ile        | att<br>Ile        | gga<br>Gly<br>440 | cag<br>Gln        | cag<br>Gln        | aac<br>Asn        | 1409 |
| atc<br>Ile        | gtg<br>Val        | ttt<br>Phe<br>445 | cat<br>His        | aat<br>Asn        | gga<br>Gly        | aag<br>Lys        | gtt<br>Val<br>450 | cct<br>Pro        | gct<br>Ala        | gga<br>Gly        | gaa<br>Glu        | aac<br>Asn<br>455 | gct<br>Ala        | gat<br>Asp        | tgg<br>Trp        | 1457 |
| caa<br>Gln<br>460 | agg<br>Arg        | cac<br>His        | ttc<br>Phe        | aga<br>Arg        | gac<br>Asp        | caa<br>Gln<br>465 | agg<br>Arg        | atg<br>Met        | ctt<br>Leu        | acc<br>Thr        | act<br>Thr<br>470 | ccg<br>Pro        | agc<br>Ser        | gat<br>Asp        | ggc<br>Gly        | 1505 |
| ctc<br>Leu<br>475 | gat<br>Asp        | cgt<br>Arg        | tgg<br>Trp        | gct<br>Ala        | gtc<br>Val<br>480 | atc<br>Ile        | gcg<br>Ala        | ccg<br>Pro        | caa<br>Gln        | agg<br>Arg<br>485 | aat<br>Asn        | tcc<br>Ser        | cat<br>His        | gaa<br>Glu        | ctc<br>Leu<br>490 | 1553 |
| cga<br>Arg        | act<br>Thr        | cta<br>Leu        | ctt<br>Leu        | gac<br>Asp<br>495 | tct<br>Ser        | ttg<br>Leu        | tat<br>Tyr        | aga<br>Arg        | gca<br>Ala<br>500 | gct<br>Ala        | agt<br>Ser        | gga<br>Gly        | atg<br>Met        | ggg<br>Gly<br>505 | ctt<br>Leu        | 1601 |
| aga<br>Arg        | att<br>Ile        | cga<br>Arg        | agc<br>Ser        | ccc<br>Pro        | cag<br>Gln        | gaa<br>Glu        | ttc<br>Phe        | ata<br>Ile<br>515 | att<br>Ile        | tat<br>Tyr        | gat<br>Asp        | gat<br>Asp        | cgc<br>Arg<br>520 | act<br>Thr        | gga<br>Gly        | 1649 |
| act               | tat               | gtg               | aga               | gca               | atg               | gat               | gat               | tgt               | gtg               | cgc               | tca               | gat               | ccc               | aaa               | ctt               | 1697 |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| Thr | Tyr | Val | Arg | Ala | Met | Asp | Asp | Cys | Val | Arg | Ser | Asp | Pro | Lys | Leu |      |
|     |     | 525 |     |     |     |     | 530 |     |     |     |     | 535 |     |     |     |      |
| ata | tta | tgc | ctc | gta | ccc | aat | gat | aac | gcc | gaa | aga | tac | tca | tca | atc | 1745 |
| Ile | Leu | Cys | Leu | Val | Pro | Asn | Asp | Asn | Ala | Glu | Arg | Tyr | Ser | Ser | Ile |      |
|     | 540 |     |     |     |     | 545 |     |     |     |     | 550 |     |     |     |     |      |
| aaa | aag | aga | gga | tac | gtt | gac | agg | gcg | gtg | cca | act | caa | gtt | gtg | acc | 1793 |
| Lys | Lys | Arg | Gly | Tyr | Val | Asp | Arg | Ala | Val | Pro | Thr | Gln | Val | Val | Thr |      |
|     | 555 |     |     |     | 560 |     |     |     |     | 565 |     |     |     |     | 570 |      |
| ctt | aaa | acg | acc | aag | aac | cgt | agc | ctt | atg | agc | att | gcc | acc | aaa | ata | 1841 |
| Leu | Lys | Thr | Thr | Lys | Asn | Arg | Ser | Leu | Met | Ser | Ile | Ala | Thr | Lys | Ile |      |
|     |     |     |     | 575 |     |     |     |     | 580 |     |     |     |     | 585 |     |      |
| gca | atc | caa | ctg | aat | tgc | aag | ttg | gga | tat | aca | ccc | tgg | atg | atc | gaa | 1889 |
| Ala | Ile | Gln | Leu | Asn | Cys | Lys | Leu | Gly | Tyr | Thr | Pro | Trp | Met | Ile | Glu |      |
|     |     |     | 590 |     |     |     |     | 595 |     |     |     |     | 600 |     |     |      |
| cta | ccc | ttg | tcc | gga | ctg | atg | aca | att | ggc | ttt | gac | att | gcg | aag | agc | 1937 |
| Leu | Pro | Leu | Ser | Gly | Leu | Met | Thr | Ile | Gly | Phe | Asp | Ile | Ala | Lys | Ser |      |
|     |     | 605 |     |     |     |     | 610 |     |     |     |     | 615 |     |     |     |      |
| aca | cga | gat | cgg | aag | agg | gcc | tac | gga | gca | ttg | att | gcc | tca | atg | gat | 1985 |
| Thr | Arg | Asp | Arg | Lys | Arg | Ala | Tyr | Gly | Ala | Leu | Ile | Ala | Ser | Met | Asp |      |
|     |     | 620 |     |     |     | 625 |     |     |     |     | 630 |     |     |     |     |      |
| cta | cag | caa | aac | tcc | acg | tac | ttc | agc | aca | gtc | acg | gag | tgc | agc | gcc | 2033 |
| Leu | Gln | Gln | Asn | Ser | Thr | Tyr | Phe | Ser | Thr | Val | Thr | Glu | Cys | Ser | Ala |      |
|     |     |     |     | 640 |     |     |     |     |     | 645 |     |     |     |     | 650 |      |
| ttt | gat | gtg | ctc | gct | aac | acc | ctt | tgg | ccg | atg | ata | gca | aag | gcc | ctg | 2081 |
| Phe | Asp | Val | Leu | Ala | Asn | Thr | Leu | Trp | Pro | Met | Ile | Ala | Lys | Ala | Leu |      |
|     |     |     |     | 655 |     |     |     | 660 |     |     |     |     |     | 665 |     |      |
| cgc | caa | tat | caa | cat | gag | cat | agg | aag | ctg | cca | tct | cga | atc | gta | ttt | 2129 |
| Arg | Gln | Tyr | Gln | His | Glu | His | Arg | Lys | Leu | Pro | Ser | Arg | Ile | Val | Phe |      |
|     |     |     | 670 |     |     |     |     | 675 |     |     |     |     | 680 |     |     |      |
| tat | cga | gac | ggt | gtg | agc | tcc | ggc | tct | cta | aag | cag | ctt | ttt | gaa | ttt | 2177 |
| Tyr | Arg | Asp | Gly | Val | Ser | Ser | Gly | Ser | Leu | Lys | Gln | Leu | Phe | Glu | Phe |      |
|     |     | 685 |     |     |     |     | 690 |     |     |     |     | 695 |     |     |     |      |
| gaa | gtc | aag | gac | atc | att | gag | aag | ttg | aaa | act | gaa | tac | gcc | cgc | gtc | 2225 |
| Glu | Val | Lys | Asp | Ile | Ile | Glu | Lys | Leu | Lys | Thr | Glu | Tyr | Ala | Arg | Val |      |
|     |     | 700 |     |     |     | 705 |     |     |     |     | 710 |     |     |     |     |      |
| cag | cta | agc | cca | ccg | caa | tta | gct | tat | att | gtg | gta | acc | aga | tcc | atg | 2273 |
| Gln | Leu | Ser | Pro | Pro | Gln | Leu | Ala | Tyr | Ile | Val | Val | Thr | Arg | Ser | Met |      |
|     |     |     |     |     | 720 |     |     |     |     | 725 |     |     |     |     | 730 |      |
| aac | acg | cgc | ttc | ttc | ctc | aac | gga | caa | aat | cct | ccg | cct | ggt | act | ata | 2321 |
| Asn | Thr | Arg | Phe | Phe | Leu | Asn | Gly | Gln | Asn | Pro | Pro | Pro | Gly | Thr | Ile |      |
|     |     |     |     | 735 |     |     |     |     | 740 |     |     |     |     | 745 |     |      |
| gtt | gat | gac | gtt | ata | act | ctg | ccc | gag | aga | tac | gac | ttt | tat | ctg | gtc | 2369 |
| Val | Asp | Asp | Val | Ile | Thr | Leu | Pro | Glu | Arg | Tyr | Asp | Phe | Tyr | Leu | Val |      |
|     |     |     | 750 |     |     |     |     | 755 |     |     |     |     | 760 |     |     |      |
| tcg | caa | caa | gtt | cgt | cag | ggt | aca | gtg | tcg | ccg | acc | agc | tac | aat | gtt | 2417 |
| Ser | Gln | Gln | Val | Arg | Gln | Gly | Thr | Val | Ser | Pro | Thr | Ser | Tyr | Asn | Val |      |

| 765   | 770 | 775 |      |
|---|-----|-----|------|
| ctt tat agc agc atg ggt ntc tca ccg gag aaa atg caa aaa ctt acg   |     |     | 2465 |
| Leu Tyr Ser Ser Met Gly Xaa Ser Pro Glu Lys Met Gln Lys Leu Thr   |     |     |      |
| 780   | 785 | 790 |      |
| tac aag atg tgc cac ttg tac tac aat tgg tcg ggc acc aca cga gtg   |     |     | 2513 |
| Tyr Lys Met Cys His Leu Tyr Tyr Asn Trp Ser Gly Thr Thr Arg Val   |     |     |      |
| 795   | 800 | 805 | 810  |
| cca gca gtt tgc cag tac gct aag aag cta gct acc ctc gtg ggt acg   |     |     | 2561 |
| Pro Ala Val Cys Gln Tyr Ala Lys Lys Leu Ala Thr Leu Val Gly Thr   |     |     |      |
|   | 815 | 820 | 825  |
| aac ttg cac tct att ccg caa aac gcg ctc gaa aag aag ttt tat tat   |     |     | 2609 |
| Asn Leu His Ser Ile Pro Gln Asn Ala Leu Glu Lys Lys Phe Tyr Tyr   |     |     |      |
|   | 830 | 835 | 840  |
| cta taattggata taatttagaa tggagtatta atccttacta agaggccata        |     |     | 2662 |
| Leu   |     |     |      |
| tatgaaacta gccagacat ttatactttt tcaatacttc cttacttttg ctaagcactt  |     |     | 2722 |
| cagcatttat gactaaatat tttgtatttg aaatgcatta ctgctctttt ttcaaacaaa |     |     | 2782 |
| agcaaaattg aggattaaga ttctggtatt taagcataag accagaggaa attcccaaac |     |     | 2842 |
| aaacatttaa agttatctat caagacatgt tcattaattt ggaatataat tactttat   |     |     | 2902 |
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 Arg Ala Met Ser Ser Tyr Thr Arg Met Asn Pro Lys Gln Arg Thr Asp  
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 405 410 415  
 Lys Val Leu Arg Asp Trp Asn Met Glu Leu Asp Lys Asn Val Thr Glu  
 420 425 430  
 Val Gln Gly Arg Ile Ile Gly Gln Gln Asn Ile Val Phe His Asn Gly  
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 450 455 460  
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 Gly Thr Val Ser Pro Thr Ser Tyr Asn Val Leu Tyr Ser Ser Met Gly  
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 agcacggggc caggatagga ctggacgctg ctggaccacg acgatcaggg agtgaccccc 120  
 accagcatcc agcctgcggc agttgttagga ctggaaggag gccaaagctga acacctgagc 180  
 tgactggaaa atg act ggc cga gcc cga gct cgg gcc cgc ggc agg gca 229  
           Met Thr Gly Arg Ala Arg Ala Arg Ala Arg Gly Arg Ala  
           1                  5                  10  
 cga ggt cag gag acg gtg cag cat gtt ggg gct gct gcg agc cag caa 277  
 Arg Gly Gln Glu Thr Val Gln His Val Gly Ala Ala Ala Ser Gln Gln  
           15                  20                  25  
 cct ggg tac atc cca ccg aga cct caa cag tcc ccc aca gag ggg gac 325  
 Pro Gly Tyr Ile Pro Pro Arg Pro Gln Gln Ser Pro Thr Glu Gly Asp  
           30                  35                  40                  45  
 ttg gtt ggc cga gga cga cag agg ggg atg gta gtc gga gcc aca tcc 373  
 Leu Val Gly Arg Gly Arg Gln Arg Gly Met Val Val Gly Ala Thr Ser  
                   50                  55                  60  
 aag tca caa gaa ctg cag atc tca gct ggg ttt cag gag ctg tca ctg 421  
 Lys Ser Gln Glu Leu Gln Ile Ser Ala Gly Phe Gln Glu Leu Ser Leu  
                   65                  70                  75  
 gca gag aga gga ggg cgt cgc cga gac ttc cat gac ntt ggt gtg aac 469  
 Ala Glu Arg Gly Gly Arg Arg Asp Phe His Asp Xaa Gly Val Asn  
                   80                  85                  90  
 acc aga cag aac ctt gac cat gtc aaa gag tca aag aca ggc tcc tct 517  
 Thr Arg Gln Asn Leu Asp His Val Lys Glu Ser Lys Thr Gly Ser Ser  
                   95                  100                  105  
 ggc atc att gtg aag ctg agc acc aac cac ttc cgg ctg acc tcg cgc 565  
 Gly Ile Ile Val Lys Leu Ser Thr Asn His Phe Arg Leu Thr Ser Arg  
           110                  115                  120                  125  
 cca cag tgg gcc ctg tat cag tac cac atc gac tac aat ccc ctg atg 613  
 Pro Gln Trp Ala Leu Tyr Gln Tyr His Ile Asp Tyr Asn Pro Leu Met  
                   130                  135                  140  
 gag gcc cga agg ctt cgc tcc gca ctg ctc ttc cag cat gaa gac ctc 661  
 Glu Ala Arg Arg Leu Arg Ser Ala Leu Leu Phe Gln His Glu Asp Leu  
                   145                  150                  155  
 att gga agg tgt cat gct ttc gat ggg aca ata ttg ttt tta cct aag 709  
 Ile Gly Arg Cys His Ala Phe Asp Gly Thr Ile Leu Phe Leu Pro Lys  
                   160                  165                  170  
 aga cta cag cac aag gtc aca gaa gta ttc agt cag act cgg aat ggg 757  
 Arg Leu Gln His Lys Val Thr Glu Val Phe Ser Gln Thr Arg Asn Gly  
                   175                  180                  185  
 gaa cac gtg agg atc acc atc acc ctg acc aac gag ctg ccg ccc acc 805  
 Glu His Val Arg Ile Thr Ile Thr Leu Thr Asn Glu Leu Pro Pro Thr  
                   190                  195                  200                  205  
 tcg ccc acc tgc ctg cag ttc tat aac atc ntc ttc agg agg ctc ttg 853

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |      |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|
| Ser | Pro | Thr | Cys | Leu | Gln | Phe | Tyr | Asn | Ile | Xaa | Phe | Arg | Arg | Leu | Leu |      |
|     |     |     |     | 210 |     |     |     |     | 215 |     |     |     |     | 220 |     |      |
| aaa | atc | atg | aat | ttg | caa | caa | att | gga | cgg | aat | tat | tac | aat | cca | agt | 901  |
| Lys | Ile | Met | Asn | Leu | Gln | Gln | Ile | Gly | Arg | Asn | Tyr | Tyr | Asn | Pro | Ser |      |
|     |     |     | 225 |     |     |     |     | 230 |     |     |     |     | 235 |     |     |      |
| gac | ccg | att | gat | att | cca | aac | cac | agg | ttg | gtg | atc | tgg | ccc | ggc | ttc | 949  |
| Asp | Pro | Ile | Asp | Ile | Pro | Asn | His | Arg | Leu | Val | Ile | Trp | Pro | Gly | Phe |      |
|     |     | 240 |     |     |     |     | 245 |     |     |     |     | 250 |     |     |     |      |
| acc | acc | tcc | atc | ctt | cag | tat | gag | aac | aac | atc | atg | ctc | tgc | aca | gac | 997  |
| Thr | Thr | Ser | Ile | Leu | Gln | Tyr | Glu | Asn | Asn | Ile | Met | Leu | Cys | Thr | Asp |      |
|     | 255 |     |     |     |     | 260 |     |     |     |     | 265 |     |     |     |     |      |
| gtc | agc | cac | aag | gtg | ctc | cgc | agc | gag | act | gtc | cta | gac | ttc | atg | ttc | 1045 |
| Val | Ser | His | Lys | Val | Leu | Arg | Ser | Glu | Thr | Val | Leu | Asp | Phe | Met | Phe |      |
| 270 |     |     |     |     | 275 |     |     |     |     | 280 |     |     |     |     | 285 |      |
| aat | cta | tac | cag | cag | aca | gag | gag | cac | aag | ttc | cag | gag | caa | gtg | tcg | 1093 |
| Asn | Leu | Tyr | Gln | Gln | Thr | Glu | Glu | His | Lys | Phe | Gln | Glu | Gln | Val | Ser |      |
|     |     |     | 290 |     |     |     |     |     | 295 |     |     |     |     | 300 |     |      |
| aag | gag | ctc | ata | ggc | ctc | atc | gtt | ctc | acc | aag | tac | aat | aac | aag | acc | 1141 |
| Lys | Glu | Leu | Ile | Gly | Leu | Ile | Val | Leu | Thr | Lys | Tyr | Asn | Asn | Lys | Thr |      |
|     |     |     | 305 |     |     |     |     | 310 |     |     |     |     | 315 |     |     |      |
| tac | cgg | gtg | gat | gac | att | gac | tgg | gac | cag | aat | cca | aag | agc | acc | ttc | 1189 |
| Tyr | Arg | Val | Asp | Asp | Ile | Asp | Trp | Asp | Gln | Asn | Pro | Lys | Ser | Thr | Phe |      |
|     |     | 320 |     |     |     |     | 325 |     |     |     |     | 330 |     |     |     |      |
| aag | aag | gcg | gat | ggc | tcg | gag | gtc | agc | ttc | ctg | gag | tac | tac | agg | aag | 1237 |
| Lys | Lys | Ala | Asp | Gly | Ser | Glu | Val | Ser | Phe | Leu | Glu | Tyr | Tyr | Arg | Lys |      |
|     | 335 |     |     |     |     | 340 |     |     |     |     | 345 |     |     |     |     |      |
| caa | tac | aac | cag | gag | atc | acg | gac | ctg | aag | cag | ccg | gtg | ctg | gtg | agc | 1285 |
| Gln | Tyr | Asn | Gln | Glu | Ile | Thr | Asp | Leu | Lys | Gln | Pro | Val | Leu | Val | Ser |      |
| 350 |     |     |     |     | 355 |     |     |     |     | 360 |     |     |     |     | 365 |      |
| caa | ccc | aag | cgg | agg | aga | ggc | ccc | ggc | ggc | acc | ctg | cct | ggc | cca | gct | 1333 |
| Gln | Pro | Lys | Arg | Arg | Arg | Gly | Pro | Gly | Gly | Thr | Leu | Pro | Gly | Pro | Ala |      |
|     |     |     |     | 370 |     |     |     | 375 |     |     |     |     |     | 380 |     |      |
| atg | ntc | atc | cct | gaa | ctc | tgc | tat | ctc | aca | ggc | ctg | act | gat | aaa | atg | 1381 |
| Met | Xaa | Ile | Pro | Glu | Leu | Cys | Tyr | Leu | Thr | Gly | Leu | Thr | Asp | Lys | Met |      |
|     |     |     | 385 |     |     |     |     | 390 |     |     |     |     | 395 |     |     |      |
| cgc | aat | gat | ttc | aat | gtg | atg | aag | gac | ctg | gca | gtg | cac | acg | cgg | ctg | 1429 |
| Arg | Asn | Asp | Phe | Asn | Val | Met | Lys | Asp | Leu | Ala | Val | His | Thr | Arg | Leu |      |
|     |     | 400 |     |     |     |     | 405 |     |     |     |     | 410 |     |     |     |      |
| acc | cct | gag | cag | cgg | cag | cgg | gag | gtg | ggc | cgc | ctc | atc | gac | tac | atc | 1477 |
| Thr | Pro | Glu | Gln | Arg | Gln | Arg | Glu | Val | Gly | Arg | Leu | Ile | Asp | Tyr | Ile |      |
|     | 415 |     |     |     |     | 420 |     |     |     |     | 425 |     |     |     |     |      |
| cac | aag | gat | gac | aat | gtg | cag | aga | gag | ctt | cga | gac | tgg | ggc | ctg | agc | 1525 |
| His | Lys | Asp | Asp | Asn | Val | Gln | Arg | Glu | Leu | Arg | Asp | Trp | Gly | Leu | Ser |      |
| 430 |     |     |     |     | 435 |     |     |     |     | 440 |     |     |     |     | 445 |      |
| ttc | gac | tca | aac | ttg | ctg | tcc | ttc | tct | gga | aga | atc | tta | caa | tct | gag | 1573 |
| Phe | Asp | Ser | Asn | Leu | Leu | Ser | Phe | Ser | Gly | Arg | Ile | Leu | Gln | Ser | Glu |      |

| 450   |      |     |     |  |  |  |  |  |  | 455 |  |  |  |  |  |  |  |  |  | 460 |  |  |  |  |  |  |  |  |  |  |
|---|------|-----|-----|--|--|--|--|--|--|-----|--|--|--|--|--|--|--|--|--|-----|--|--|--|--|--|--|--|--|--|--|
| aag atc cac cag ggc gga aag acg ttt gat tac aac cca caa ttt gca | 1621 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Lys Ile His Gln Gly Gly Lys Thr Phe Asp Tyr Asn Pro Gln Phe Ala |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 465   | 470  | 475 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gac tgg tcc aaa gaa aca aga ggc gcg ccg ctg atc agc gtg aag cca | 1669 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Asp Trp Ser Lys Glu Thr Arg Gly Ala Pro Leu Ile Ser Val Lys Pro |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 480   | 485  | 490 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| ttg gat aac tgg ctg ctg atc tat acc cgc agg aat tat gaa gca gcc | 1717 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Leu Asp Asn Trp Leu Leu Ile Tyr Thr Arg Arg Asn Tyr Glu Ala Ala |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 495   | 500  | 505 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| aac tca ctg ata cag aac ctg ttc aaa gtg act cca gcc atg ggc atc | 1765 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Asn Ser Leu Ile Gln Asn Leu Phe Lys Val Thr Pro Ala Met Gly Ile |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 510   | 515  | 520 | 525 |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| cag atg aaa aag gca atc atg atc gag gtg gat gac aga aca gaa gct | 1813 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Gln Met Lys Lys Ala Ile Met Ile Glu Val Asp Asp Arg Thr Glu Ala |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 530   | 535  | 540 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| tat ctg aga gcc ttg cag cag aag gtg acg tca gac act cag ata gtt | 1861 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Tyr Leu Arg Ala Leu Gln Gln Lys Val Thr Ser Asp Thr Gln Ile Val |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 545   | 550  | 555 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gtc tgt ctc ttg tca agt aat cgg aag gac aaa tat gat gcc atc aag | 1909 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Val Cys Leu Leu Ser Ser Asn Arg Lys Asp Lys Tyr Asp Ala Ile Lys |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 560   | 565  | 570 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| aag tac ttg tgt aca gac tgc ccc acc cca agt cag tgt gtg gtg gcc | 1957 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Lys Tyr Leu Cys Thr Asp Cys Pro Thr Pro Ser Gln Cys Val Val Ala |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 575   | 580  | 585 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| cgg acc ctg ggc aag cag caa aca gtc atg gcc att gcc acc aag atc | 2005 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Arg Thr Leu Gly Lys Gln Gln Thr Val Met Ala Ile Ala Thr Lys Ile |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 590   | 595  | 600 | 605 |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gcc ctg cag atg aac tgc aag atg gga ggc gag ctc tgg cgg gtg gac | 2053 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Ala Leu Gln Met Asn Cys Lys Met Gly Gly Glu Leu Trp Arg Val Asp |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 610   | 615  | 620 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| atg gcc ctg aaa ctg gca atg atc gtg ggc atc gac tgt tac cat gac | 2101 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Met Ala Leu Lys Leu Ala Met Ile Val Gly Ile Asp Cys Tyr His Asp |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 625   | 630  | 635 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| acc aca gct ggg cgg agg tcc atc gca gga ttc gtc gcc agc atc aat | 2149 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Thr Thr Ala Gly Arg Arg Ser Ile Ala Gly Phe Val Ala Ser Ile Asn |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 640   | 645  | 650 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gaa ggg atg acc cgc tgg ttc tcc cgc tgc gtc ttt cag gac cgc ggg | 2197 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Glu Gly Met Thr Arg Trp Phe Ser Arg Cys Val Phe Gln Asp Arg Gly |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 655   | 660  | 665 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| cag gag ctg gtg gat ggt ctc aag gtg tgc ttg caa gct gct ctg agg | 2245 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Gln Glu Leu Val Asp Gly Leu Lys Val Cys Leu Gln Ala Ala Leu Arg |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 670   | 675  | 680 | 685 |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gct tgg agt ggc tgc aat gaa tac atg ccc agc cgt gtc atc gtg tac | 2293 |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Ala Trp Ser Gly Cys Asn Glu Tyr Met Pro Ser Arg Val Ile Val Tyr |      |     |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 690   | 695  | 700 |     |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |     |  |  |  |  |  |  |  |  |  |  |

cga gac ggt gtg ggg gac ggg cag ctg aag acc ctg gtc aat tat gag 2341  
 Arg Asp Gly Val Gly Asp Gly Gln Leu Lys Thr Leu Val Asn Tyr Glu  
 705 710 715

gtc cca cag ttc cta gat tgc ctc aag tca gtc ggg aga ggt tac aac 2389  
 Val Pro Gln Phe Leu Asp Cys Leu Lys Ser Val Gly Arg Gly Tyr Asn  
 720 725 730

cca aga ctg act gta atc gtg gtg aag aag cgt gtc aat gcc agg ttt 2437  
 Pro Arg Leu Thr Val Ile Val Val Lys Lys Arg Val Asn Ala Arg Phe  
 735 740 745

ttt gct cag tct ggg gga aga ctt cag aac cct ctt cca ggg aca gtc 2485  
 Phe Ala Gln Ser Gly Gly Arg Leu Gln Asn Pro Leu Pro Gly Thr Val  
 750 755 760 765

atc gat gtg gaa gtc acc aga cca gag tgg tat gac ttt ttc atc gtg 2533  
 Ile Asp Val Glu Val Thr Arg Pro Glu Trp Tyr Asp Phe Phe Ile Val  
 770 775 780

agc cag gca gtg aga agc ggg agt gtg tcc cca aca cac tac aat gtc 2581  
 Ser Gln Ala Val Arg Ser Gly Ser Val Ser Pro Thr His Tyr Asn Val  
 785 790 795

atc tat gac agc agt ggc ctg aag ccc gac cac atc cag cgg ctg aca 2629  
 Ile Tyr Asp Ser Ser Gly Leu Lys Pro Asp His Ile Gln Arg Leu Thr  
 800 805 810

tac aag ntc tgc cac gtg tac tat aat tgg cct gga gtc atc cga gtc 2677  
 Tyr Lys Xaa Cys His Val Tyr Tyr Asn Trp Pro Gly Val Ile Arg Val  
 815 820 825

cct gca cct tgc cag tat gca cac aag ctg gcc ttc ctc gtg ggc cag 2725  
 Pro Ala Pro Cys Gln Tyr Ala His Lys Leu Ala Phe Leu Val Gly Gln  
 830 835 840 845

agc atc cac aga gag cca aac ctc tcc ctg tcc aac cgc ctc tac tac 2773  
 Ser Ile His Arg Glu Pro Asn Leu Ser Leu Ser Asn Arg Leu Tyr Tyr  
 850 855 860

ctc taaccagcag cgagggccgg catgctggtt tccttcagag ctctgcccaa 2826  
 Leu

tccttcagtt ctatttttca taggatgagg ttctagcggg atgttggggg taggggttgg 2886

gggccgctgt tttgttttgt tttgttttta gttgttggtg tgtagcggct atagagttaa 2946

ctaaggctta tgtttgcttt gtttctcatg gtgtgttggtg acagtttget tggcagagtg 3006

gtggcaaggg ccgtggtacc acagatagac tttcctaaag cagccgtggt ggcaggttct 3066

tggaggtgct cctgggagca cctcctattg tacgctgctc tctctctctc tctctctctc 3126

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acaaggcaag aatgcccgaga gcacccctaga tgggtgctat atgggactct gacacctcag 3246

gttcttaaag ataaaaaggc cagaggtacc tttctgtaat tcttttaaga gttaggtcat 3306

aaggaatgaa aagagttact tttctccctc catgaaagtg ttttttaaga ctgacaaggc 3366

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 cagcctaggc tacatagtga gactttgtct taacaaacag aaaaaaagaa aaagaaagaa 3666  
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 gacaaagaga gcagcttaga gtggctagag tgtgatgagt tttacacaat ggcgatgtgt 3906  
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 35 40 45

Arg Gly Arg Gln Arg Gly Met Val Val Gly Ala Thr Ser Lys Ser Gln  
 50 55 60  
 Glu Leu Gln Ile Ser Ala Gly Phe Gln Glu Leu Ser Leu Ala Glu Arg  
 65 70 75 80  
 Gly Gly Arg Arg Arg Asp Phe His Asp Xaa Gly Val Asn Thr Arg Gln  
 85 90 95  
 Asn Leu Asp His Val Lys Glu Ser Lys Thr Gly Ser Ser Gly Ile Ile  
 100 105 110  
 Val Lys Leu Ser Thr Asn His Phe Arg Leu Thr Ser Arg Pro Gln Trp  
 115 120 125  
 Ala Leu Tyr Gln Tyr His Ile Asp Tyr Asn Pro Leu Met Glu Ala Arg  
 130 135 140  
 Arg Leu Arg Ser Ala Leu Leu Phe Gln His Glu Asp Leu Ile Gly Arg  
 145 150 155 160  
 Cys His Ala Phe Asp Gly Thr Ile Leu Phe Leu Pro Lys Arg Leu Gln  
 165 170 175  
 His Lys Val Thr Glu Val Phe Ser Gln Thr Arg Asn Gly Glu His Val  
 180 185 190  
 Arg Ile Thr Ile Thr Leu Thr Asn Glu Leu Pro Pro Thr Ser Pro Thr  
 195 200 205  
 Cys Leu Gln Phe Tyr Asn Ile Xaa Phe Arg Arg Leu Leu Lys Ile Met  
 210 215 220  
 Asn Leu Gln Gln Ile Gly Arg Asn Tyr Tyr Asn Pro Ser Asp Pro Ile  
 225 230 235 240  
 Asp Ile Pro Asn His Arg Leu Val Ile Trp Pro Gly Phe Thr Thr Ser  
 245 250 255  
 Ile Leu Gln Tyr Glu Asn Asn Ile Met Leu Cys Thr Asp Val Ser His  
 260 265 270  
 Lys Val Leu Arg Ser Glu Thr Val Leu Asp Phe Met Phe Asn Leu Tyr  
 275 280 285  
 Gln Gln Thr Glu Glu His Lys Phe Gln Glu Gln Val Ser Lys Glu Leu  
 290 295 300  
 Ile Gly Leu Ile Val Leu Thr Lys Tyr Asn Asn Lys Thr Tyr Arg Val  
 305 310 315 320  
 Asp Asp Ile Asp Trp Asp Gln Asn Pro Lys Ser Thr Phe Lys Lys Ala  
 325 330 335  
 Asp Gly Ser Glu Val Ser Phe Leu Glu Tyr Tyr Arg Lys Gln Tyr Asn  
 340 345 350  
 Gln Glu Ile Thr Asp Leu Lys Gln Pro Val Leu Val Ser Gln Pro Lys  
 355 360 365  
 Arg Arg Arg Gly Pro Gly Gly Thr Leu Pro Gly Pro Ala Met Xaa Ile

|   |                                     |                         |
|---|-------------------------------------|-------------------------|
| 370   | 375                                 | 380                     |
| Pro Glu Leu Cys Tyr   | Leu Thr Gly Leu Thr                 | Asp Lys Met Arg Asn Asp |
| 385   | 390                                 | 395 400                 |
| Phe Asn Val Met Lys   | Asp Leu Ala Val His Thr Arg Leu Thr | Pro Glu                 |
| 405   | 410                                 | 415                     |
| Gln Arg Gln Arg Glu Val Gly Arg                                 | Leu Ile Asp Tyr Ile His Lys Asp     |                         |
| 420   | 425                                 | 430                     |
| Asp Asn Val Gln Arg Glu Leu Arg                                 | Asp Trp Gly Leu Ser Phe Asp Ser     |                         |
| 435   | 440                                 | 445                     |
| Asn Leu Leu Ser Phe Ser Gly Arg Ile Leu Gln Ser Glu Lys Ile His |                                     |                         |
| 450   | 455                                 | 460                     |
| Gln Gly Gly Lys Thr Phe Asp Tyr Asn Pro Gln Phe Ala Asp Trp Ser |                                     |                         |
| 465   | 470                                 | 475 480                 |
| Lys Glu Thr Arg Gly Ala Pro Leu Ile Ser Val Lys Pro Leu Asp Asn |                                     |                         |
| 485   | 490                                 | 495                     |
| Trp Leu Leu Ile Tyr Thr Arg Arg Asn Tyr Glu Ala Ala Asn Ser Leu |                                     |                         |
| 500   | 505                                 | 510                     |
| Ile Gln Asn Leu Phe Lys Val Thr Pro Ala Met Gly Ile Gln Met Lys |                                     |                         |
| 515   | 520                                 | 525                     |
| Lys Ala Ile Met Ile Glu Val Asp Asp Arg Thr Glu Ala Tyr Leu Arg |                                     |                         |
| 530   | 535                                 | 540                     |
| Ala Leu Gln Gln Lys Val Thr Ser Asp Thr Gln Ile Val Val Cys Leu |                                     |                         |
| 545   | 550                                 | 555 560                 |
| Leu Ser Ser Asn Arg Lys Asp Lys Tyr Asp Ala Ile Lys Lys Tyr Leu |                                     |                         |
| 565   | 570                                 | 575                     |
| Cys Thr Asp Cys Pro Thr Pro Ser Gln Cys Val Val Ala Arg Thr Leu |                                     |                         |
| 580   | 585                                 | 590                     |
| Gly Lys Gln Gln Thr Val Met Ala Ile Ala Thr Lys Ile Ala Leu Gln |                                     |                         |
| 595   | 600                                 | 605                     |
| Met Asn Cys Lys Met Gly Gly Glu Leu Trp Arg Val Asp Met Ala Leu |                                     |                         |
| 610   | 615                                 | 620                     |
| Lys Leu Ala Met Ile Val Gly Ile Asp Cys Tyr His Asp Thr Thr Ala |                                     |                         |
| 625   | 630                                 | 635 640                 |
| Gly Arg Arg Ser Ile Ala Gly Phe Val Ala Ser Ile Asn Glu Gly Met |                                     |                         |
| 645   | 650                                 | 655                     |
| Thr Arg Trp Phe Ser Arg Cys Val Phe Gln Asp Arg Gly Gln Glu Leu |                                     |                         |
| 660   | 665                                 | 670                     |
| Val Asp Gly Leu Lys Val Cys Leu Gln Ala Ala Leu Arg Ala Trp Ser |                                     |                         |
| 675   | 680                                 | 685                     |
| Gly Cys Asn Glu Tyr Met Pro Ser Arg Val Ile Val Tyr Arg Asp Gly |                                     |                         |
| 690   | 695                                 | 700                     |

Val Gly Asp Gly Gln Leu Lys Thr Leu Val Asn Tyr Glu Val Pro Gln  
 705 710 715 720  
 Phe Leu Asp Cys Leu Lys Ser Val Gly Arg Gly Tyr Asn Pro Arg Leu  
 725 730 735  
 Thr Val Ile Val Val Lys Lys Arg Val Asn Ala Arg Phe Phe Ala Gln  
 740 745 750  
 Ser Gly Gly Arg Leu Gln Asn Pro Leu Pro Gly Thr Val Ile Asp Val  
 755 760 765  
 Glu Val Thr Arg Pro Glu Trp Tyr Asp Phe Phe Ile Val Ser Gln Ala  
 770 775 780  
 Val Arg Ser Gly Ser Val Ser Pro Thr His Tyr Asn Val Ile Tyr Asp  
 785 790 795 800  
 Ser Ser Gly Leu Lys Pro Asp His Ile Gln Arg Leu Thr Tyr Lys Xaa  
 805 810 815  
 Cys His Val Tyr Tyr Asn Trp Pro Gly Val Ile Arg Val Pro Ala Pro  
 820 825 830  
 Cys Gln Tyr Ala His Lys Leu Ala Phe Leu Val Gly Gln Ser Ile His  
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 aggaccagga ctagggcgag ggcagcggtc caagaaatag aaaaca atg act ggg 175



Met Thr Gly

1

|   |     |
|---|-----|
| aga gcc cga gcc aga gcc aga gga agg gcc cgc ggt cag gag aca gcg | 223 |
| Arg Ala Arg Ala Arg Ala Arg Gly Arg Ala Arg Gly Gln Glu Thr Ala |     |
| 5 10 15   |     |
| cag ctg gtg ggc tcc act gcc agt cag caa cct ggt tat att cag cct | 271 |
| Gln Leu Val Gly Ser Thr Ala Ser Gln Gln Pro Gly Tyr Ile Gln Pro |     |
| 20 25 30 35   |     |
| agg cct cag ccg cca cca gca gag ggg gaa tta ttt ggc cgt gga cgg | 319 |
| Arg Pro Gln Pro Pro Pro Ala Glu Gly Glu Leu Phe Gly Arg Gly Arg |     |
| 40 45 50  |     |
| cag aga gga aca gca gga gga aca gcc aag tca caa gga ctc cag ata | 367 |
| Gln Arg Gly Thr Ala Gly Gly Thr Ala Lys Ser Gln Gly Leu Gln Ile |     |
| 55 60 65  |     |
| tct gct gga ttt cag gag tta tcg nta gca gag aga gga ggt cgt cgt | 415 |
| Ser Ala Gly Phe Gln Glu Leu Ser Xaa Ala Glu Arg Gly Gly Arg Arg |     |
| 70 75 80  |     |
| aga gat ttt cat gat ctt ggt gtg aat aca agg cag aac cta gac cat | 463 |
| Arg Asp Phe His Asp Leu Gly Val Asn Thr Arg Gln Asn Leu Asp His |     |
| 85 90 95  |     |
| gtt aaa gaa tca aaa aca ggt tct tca ggc att ata gta agg tta agc | 511 |
| Val Lys Glu Ser Lys Thr Gly Ser Ser Gly Ile Ile Val Arg Leu Ser |     |
| 100 105 110 115   |     |
| act aac cat ttc cgg ctg aca tcc cgt ccc cag tgg gcc tta tat cag | 559 |
| Thr Asn His Phe Arg Leu Thr Ser Arg Pro Gln Trp Ala Leu Tyr Gln |     |
| 120 125 130   |     |
| tat cac att gac tat aac cca ctg atg gaa gcc aga aga ctc cgt tca | 607 |
| Tyr His Ile Asp Tyr Asn Pro Leu Met Glu Ala Arg Arg Leu Arg Ser |     |
| 135 140 145   |     |
| gct ctt ctt ttt caa cac gaa gat cta att gga aag tgt cat gct ttt | 655 |
| Ala Leu Leu Phe Gln His Glu Asp Leu Ile Gly Lys Cys His Ala Phe |     |
| 150 155 160   |     |
| gat gga acg ata tta ttt tta cct aaa aga cta cag caa aag gtt act | 703 |
| Asp Gly Thr Ile Leu Phe Leu Pro Lys Arg Leu Gln Gln Lys Val Thr |     |
| 165 170 175   |     |
| gaa gtt ttt agt aag acc cgg aat gga gag gat gtg agg ata acg atc | 751 |
| Glu Val Phe Ser Lys Thr Arg Asn Gly Glu Asp Val Arg Ile Thr Ile |     |
| 180 185 190 195   |     |
| act tta aca aat gaa ctt cca cct aca tca cca act tgt ttg cag ttc | 799 |
| Thr Leu Thr Asn Glu Leu Pro Pro Thr Ser Pro Thr Cys Leu Gln Phe |     |
| 200 205 210   |     |
| tat aat att att ttc agg agg ctt ttg aaa atc atg aat ttg caa caa | 847 |
| Tyr Asn Ile Ile Phe Arg Arg Leu Leu Lys Ile Met Asn Leu Gln Gln |     |
| 215 220 225   |     |
| att gga cga aat tat tat aac cca aat gac cca att gat att cca agt | 895 |
| Ile Gly Arg Asn Tyr Tyr Asn Pro Asn Asp Pro Ile Asp Ile Pro Ser |     |

| 230  |     |     |     |     |     |     |     |     |     | 235 |     |     |     |     |     |     |  |  |  | 240 |  |  |  |  |  |  |  |  |  |  |
|--|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|--|--|-----|--|--|--|--|--|--|--|--|--|--|
| cac  | agg | ttg | gtg | att | tgg | cct | ggc | ttc | act | act | tcc | atc | ctt | cag | tat | 943 |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| His  | Arg | Leu | Val | Ile | Trp | Pro | Gly | Phe | Thr | Thr | Ser | Ile | Leu | Gln | Tyr |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 245  |     |     |     |     | 250 |     |     |     |     | 255 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gaa aac agc atc atg ctc tgc act gac gtt agc cat aaa gtc ctt cga 991  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Glu Asn Ser Ile Met Leu Cys Thr Asp Val Ser His Lys Val Leu Arg 275  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 260  |     |     |     |     | 265 |     |     |     |     | 270 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| agt gag act gtt ttg gat ttc atg ttc aac ttt tat cat cag aca gaa 1039 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Ser Glu Thr Val Leu Asp Phe Met Phe Asn Phe Tyr His Gln Thr Glu 290  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 280  |     |     |     |     | 285 |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gaa cat aaa ttt caa gaa caa gtt tcc aaa gaa nta ata ggt tta gtt 1087 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Glu His Lys Phe Gln Glu Gln Val Ser Lys Glu Xaa Ile Gly Leu Val 305  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 295  |     |     |     |     | 300 |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gtt ctt acc aag tat aac att aag aca tac aga gtg gat gat att gac 1135 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Val Leu Thr Lys Tyr Asn Ile Lys Thr Tyr Arg Val Asp Asp Ile Asp 320  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 310  |     |     |     |     | 315 |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| tgg gac cag aat ccc aag agc acc ttt aag aaa gcc gac ggc tct ggg 1183 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Trp Asp Gln Asn Pro Lys Ser Thr Phe Lys Lys Ala Asp Gly Ser Gly 335  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 325  |     |     |     |     | 330 |     |     |     |     | 335 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gtc agc ttc tta gaa tac tac agg aag caa tac aac caa gag atc acc 1231 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Val Ser Phe Leu Glu Tyr Arg Lys Gln Tyr Asn Gln Glu Ile Thr 355      |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 340  |     |     |     |     | 345 |     |     |     |     | 350 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gac ttg aag cag cct gtc ttg gtc agc cag ccc aag aga agg cgg ggc 1279 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Asp Leu Lys Gln Pro Val Leu Val Ser Gln Pro Lys Arg Arg Arg Gly 370  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 360  |     |     |     |     | 365 |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| cct ggg ggg aca ctg cca ggg cct gcc atg ctc att cct gag ctc tgc 1327 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Pro Gly Gly Thr Leu Pro Gly Pro Ala Met Leu Ile Pro Glu Leu Cys 385  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 375  |     |     |     |     | 380 |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| tat ctt aca ggt cta act gat aaa atg cgt aat gat ttt aac gtg atg 1375 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Tyr Leu Thr Gly Leu Thr Asp Lys Met Arg Asn Asp Phe Asn Val Met 400  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 390  |     |     |     |     | 395 |     |     |     |     | 400 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| aaa gac tta gcc gtt cat aca aga cta act cca gag caa agg cag cgt 1423 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Lys Asp Leu Ala Val His Thr Arg Leu Thr Pro Glu Gln Arg Gln Arg 415  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 405  |     |     |     |     | 410 |     |     |     |     | 415 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| gaa gtg gga cga ctc att gat tac att cat aaa aac gat aat gtt caa 1471 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Glu Val Gly Arg Leu Ile Asp Tyr Ile His Lys Asn Asp Asn Val Gln 435  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 420  |     |     |     |     | 425 |     |     |     |     | 430 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| agg gag ctt cga gac tgg ggt ttg agc ttt gat tcc aac tta ctg tcc 1519 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Arg Glu Leu Arg Asp Trp Gly Leu Ser Phe Asp Ser Asn Leu Leu Ser 450  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 440  |     |     |     |     | 445 |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| ttc tca gga aga att ttg caa aca gaa aag att cac caa ggt gga aaa 1567 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Phe Ser Gly Arg Ile Leu Gln Thr Glu Lys Ile His Gln Gly Gly Lys 465  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 455  |     |     |     |     | 460 |     |     |     |     | 465 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| aca ttt gat tac aat cca caa ttt gca gat tgg tcc aaa gaa aca aga 1615 |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| Thr Phe Asp Tyr Asn Pro Gln Phe Ala Asp Trp Ser Lys Glu Thr Arg 480  |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |
| 470  |     |     |     |     | 475 |     |     |     |     | 480 |     |     |     |     |     |     |  |  |  |     |  |  |  |  |  |  |  |  |  |  |

|   |      |
|---|------|
| ggt gca cca tta att agt gtt aag cca cta gat aac tgg ctg ttg atc | 1663 |
| Gly Ala Pro Leu Ile Ser Val Lys Pro Leu Asp Asn Trp Leu Leu Ile |      |
| 485 490 495   |      |
| tat acg cga aga aat tat gaa gca gcc aat tca ttg ata caa aat cta | 1711 |
| Tyr Thr Arg Arg Asn Tyr Glu Ala Ala Asn Ser Leu Ile Gln Asn Leu |      |
| 500 505 510 515   |      |
| ttt aaa gtt aca cca gcc atg ggc atg caa atg aga aaa gca ata atg | 1759 |
| Phe Lys Val Thr Pro Ala Met Gly Met Gln Met Arg Lys Ala Ile Met |      |
| 520 525 530   |      |
| att gaa gtg gat gac aga act gaa gcc tac tta aga gtc tta cag caa | 1807 |
| Ile Glu Val Asp Asp Arg Thr Glu Ala Tyr Leu Arg Val Leu Gln Gln |      |
| 535 540 545   |      |
| aag gtc aca gca gac acc cag ata gtt gtc tgt ctg ttg tca agt aat | 1855 |
| Lys Val Thr Ala Asp Thr Gln Ile Val Val Cys Leu Leu Ser Ser Asn |      |
| 550 555 560   |      |
| cgg aag gac aaa tac gat gct att aaa aaa tac ctg tgt aca gat tgc | 1903 |
| Arg Lys Asp Lys Tyr Asp Ala Ile Lys Lys Tyr Leu Cys Thr Asp Cys |      |
| 565 570 575   |      |
| cct acc cca agt cag tgt gtg gtg gcc cga acc tta ggc aaa cag caa | 1951 |
| Pro Thr Pro Ser Gln Cys Val Val Ala Arg Thr Leu Gly Lys Gln Gln |      |
| 580 585 590 595   |      |
| act gtc atg gcc att gct aca aag att gcc cta cag atg aac tgc aag | 1999 |
| Thr Val Met Ala Ile Ala Thr Lys Ile Ala Leu Gln Met Asn Cys Lys |      |
| 600 605 610   |      |
| atg gga gga gag ctc tgg agg gtg gac atc ccc ctg aag ctc gtg atg | 2047 |
| Met Gly Gly Glu Leu Trp Arg Val Asp Ile Pro Leu Lys Leu Val Met |      |
| 615 620 625   |      |
| atc gtt ggc atc gat tgt tac cat gac atg aca gct ggg cgg agg tca | 2095 |
| Ile Val Gly Ile Asp Cys Tyr His Asp Met Thr Ala Gly Arg Arg Ser |      |
| 630 635 640   |      |
| atc gca gga ttt gtt gcc agc atc aat gaa ggg atg acc cgc tgg ttc | 2143 |
| Ile Ala Gly Phe Val Ala Ser Ile Asn Glu Gly Met Thr Arg Trp Phe |      |
| 645 650 655   |      |
| tca cgc tgc ata ttt cag gat aga gga cag gag ctg gta gat ggg ctc | 2191 |
| Ser Arg Cys Ile Phe Gln Asp Arg Gly Gln Glu Leu Val Asp Gly Leu |      |
| 660 665 670 675   |      |
| aaa gtc tgc ctg caa gcg gct ctg agg gct tgg aat agc tgc aat gag | 2239 |
| Lys Val Cys Leu Gln Ala Ala Leu Arg Ala Trp Asn Ser Cys Asn Glu |      |
| 680 685 690   |      |
| tac atg ccc agc cgg atc atc gtg tac cgc gat ggc gta gga gac ggc | 2287 |
| Tyr Met Pro Ser Arg Ile Ile Val Tyr Arg Asp Gly Val Gly Asp Gly |      |
| 695 700 705   |      |
| cag ctg aaa aca ctg gtg aac tac gaa gtg cca cag ttt ttg gat tgt | 2335 |
| Gln Leu Lys Thr Leu Val Asn Tyr Glu Val Pro Gln Phe Leu Asp Cys |      |
| 710 715 720   |      |

|  |      |
|--|------|
| cta aaa tcc att ggt aga ggt tac aac cct aga nta acg gta att gtg    | 2383 |
| Leu Lys Ser Ile Gly Arg Gly Tyr Asn Pro Arg Xaa Thr Val Ile Val    |      |
| 725 730 735  |      |
| gtg aag aaa aga gtg aac acc aga ttt ttt gct cag tct gga gga aga    | 2431 |
| Val Lys Lys Arg Val Asn Thr Arg Phe Phe Ala Gln Ser Gly Gly Arg    |      |
| 740 745 750 755  |      |
| ctt cag aat cca ctt cct gga aca gtt att gat gta gag gtt acc aga    | 2479 |
| Leu Gln Asn Pro Leu Pro Gly Thr Val Ile Asp Val Glu Val Thr Arg    |      |
| 760 765 770  |      |
| cca gaa tgg tat gac ttt ttt atc gtg agc cag gct gtg aga agt ggt    | 2527 |
| Pro Glu Trp Tyr Asp Phe Phe Ile Val Ser Gln Ala Val Arg Ser Gly    |      |
| 775 780 785  |      |
| agt gtt tct ccc aca cat tac aat gtc atc tat gac aac agc ggc ctg    | 2575 |
| Ser Val Ser Pro Thr His Tyr Asn Val Ile Tyr Asp Asn Ser Gly Leu    |      |
| 790 795 800  |      |
| aag cca gac cac ata cag cgc ttg acc tac aag ctg tgc cac atc tat    | 2623 |
| Lys Pro Asp His Ile Gln Arg Leu Thr Tyr Lys Leu Cys His Ile Tyr    |      |
| 805 810 815  |      |
| tac aac tgg cca ggt gtc att cgt gtt cct gct cct tgc cag tac gcc    | 2671 |
| Tyr Asn Trp Pro Gly Val Ile Arg Val Pro Ala Pro Cys Gln Tyr Ala    |      |
| 820 825 830 835  |      |
| cac aag ctg gct ttt ctt gtt ggc cag agt att cac aga gag cca aat    | 2719 |
| His Lys Leu Ala Phe Leu Val Gly Gln Ser Ile His Arg Glu Pro Asn    |      |
| 840 845 850  |      |
| ctg tca ctg tca aac cgc ctt tac tac ctg taacctgcag aagacgatgc      | 2769 |
| Leu Ser Leu Ser Asn Arg Leu Tyr Tyr Leu                            |      |
| 855 860  |      |
| agccgctttt ctttttgaaa tgactttggg attttttttaa gcttttattt actttttttt | 2829 |
| taactgttat ctttctggat gaaacttggg aaggggatta ggagatctag cattttattt  | 2889 |
| ctagcattgc tattcacggg cttccttatt ttatatgtaa aaattaagat tttatatattt | 2949 |
| atcttcttgt ttctcataga tattttgtga gcattttttt gtttattttg aagaaatgtg  | 3009 |
| gataagatac ttggtagtat aaaacagact ctctgagagt atttgaaatg tgtttggaga  | 3069 |
| tttacttaaa cgtactttca ggagtgcagc agtcctactt ataaacctat attaaacttta | 3129 |
| tttttgagat acctgttttg aatttaaagg agataagagg cgtaaagtag gatgctcact  | 3189 |
| acaaccatag gtgggggttc agctcatatc ttaaagataa aagggtactat tatataacct | 3249 |
| atacacaaga tacaggagaa aatatgcttg atttttattt ggcagggggg ctaggttgta  | 3309 |
| tgggagtaaa aaaaacattg aaaattttta aattgtccaa agaaacattt taagactctt  | 3369 |
| taacaaaaaa ggccatgagt aaatctctat attaacatca ctattttattt tgttttgga  | 3429 |
| ctgggacatg attctatttg ttataaaata aaattgatgt ccc                    | 3472 |

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20 25 30  
Ile Gln Pro Arg Pro Gln Pro Pro Pro Ala Glu Gly Glu Leu Phe Gly  
35 40 45  
Arg Gly Arg Gln Arg Gly Thr Ala Gly Gly Thr Ala Lys Ser Gln Gly  
50 55 60  
Leu Gln Ile Ser Ala Gly Phe Gln Glu Leu Ser Xaa Ala Glu Arg Gly  
65 70 75 80  
Gly Arg Arg Arg Asp Phe His Asp Leu Gly Val Asn Thr Arg Gln Asn  
85 90 95  
Leu Asp His Val Lys Glu Ser Lys Thr Gly Ser Ser Gly Ile Ile Val  
100 105 110  
Arg Leu Ser Thr Asn His Phe Arg Leu Thr Ser Arg Pro Gln Trp Ala  
115 120 125  
Leu Tyr Gln Tyr His Ile Asp Tyr Asn Pro Leu Met Glu Ala Arg Arg  
130 135 140  
Leu Arg Ser Ala Leu Leu Phe Gln His Glu Asp Leu Ile Gly Lys Cys  
145 150 155 160  
His Ala Phe Asp Gly Thr Ile Leu Phe Leu Pro Lys Arg Leu Gln Gln  
165 170 175  
Lys Val Thr Glu Val Phe Ser Lys Thr Arg Asn Gly Glu Asp Val Arg  
180 185 190  
Ile Thr Ile Thr Leu Thr Asn Glu Leu Pro Pro Thr Ser Pro Thr Cys  
195 200 205  
Leu Gln Phe Tyr Asn Ile Ile Phe Arg Arg Leu Leu Lys Ile Met Asn

| 210  | 215 | 220 |
|--|-----|-----|
| Leu Gln Gln Ile Gly Arg Asn Tyr Tyr Asn Pro Asn Asp Pro Ile Asp<br>225 230 235 240 |     |     |
| Ile Pro Ser His Arg Leu Val Ile Trp Pro Gly Phe Thr Thr Ser Ile<br>245 250 255     |     |     |
| Leu Gln Tyr Glu Asn Ser Ile Met Leu Cys Thr Asp Val Ser His Lys<br>260 265 270     |     |     |
| Val Leu Arg Ser Glu Thr Val Leu Asp Phe Met Phe Asn Phe Tyr His<br>275 280 285     |     |     |
| Gln Thr Glu Glu His Lys Phe Gln Glu Gln Val Ser Lys Glu Xaa Ile<br>290 295 300     |     |     |
| Gly Leu Val Val Leu Thr Lys Tyr Asn Ile Lys Thr Tyr Arg Val Asp<br>305 310 315 320 |     |     |
| Asp Ile Asp Trp Asp Gln Asn Pro Lys Ser Thr Phe Lys Lys Ala Asp<br>325 330 335     |     |     |
| Gly Ser Gly Val Ser Phe Leu Glu Tyr Tyr Arg Lys Gln Tyr Asn Gln<br>340 345 350     |     |     |
| Glu Ile Thr Asp Leu Lys Gln Pro Val Leu Val Ser Gln Pro Lys Arg<br>355 360 365     |     |     |
| Arg Arg Gly Pro Gly Gly Thr Leu Pro Gly Pro Ala Met Leu Ile Pro<br>370 375 380     |     |     |
| Glu Leu Cys Tyr Leu Thr Gly Leu Thr Asp Lys Met Arg Asn Asp Phe<br>385 390 395 400 |     |     |
| Asn Val Met Lys Asp Leu Ala Val His Thr Arg Leu Thr Pro Glu Gln<br>405 410 415     |     |     |
| Arg Gln Arg Glu Val Gly Arg Leu Ile Asp Tyr Ile His Lys Asn Asp<br>420 425 430     |     |     |
| Asn Val Gln Arg Glu Leu Arg Asp Trp Gly Leu Ser Phe Asp Ser Asn<br>435 440 445     |     |     |
| Leu Leu Ser Phe Ser Gly Arg Ile Leu Gln Thr Glu Lys Ile His Gln<br>450 455 460     |     |     |
| Gly Gly Lys Thr Phe Asp Tyr Asn Pro Gln Phe Ala Asp Trp Ser Lys<br>465 470 475 480 |     |     |
| Glu Thr Arg Gly Ala Pro Leu Ile Ser Val Lys Pro Leu Asp Asn Trp<br>485 490 495     |     |     |
| Leu Leu Ile Tyr Thr Arg Arg Asn Tyr Glu Ala Ala Asn Ser Leu Ile<br>500 505 510     |     |     |
| Gln Asn Leu Phe Lys Val Thr Pro Ala Met Gly Met Gln Met Arg Lys<br>515 520 525     |     |     |
| Ala Ile Met Ile Glu Val Asp Asp Arg Thr Glu Ala Tyr Leu Arg Val<br>530 535 540     |     |     |

|     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |     |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Leu | Gln | Gln | Lys | Val | Thr | Ala | Asp | Thr | Gln | Ile | Val | Val | Cys | Leu | Leu | 545 | 550 | 555 | 560 |
| Ser | Ser | Asn | Arg | Lys | Asp | Lys | Tyr | Asp | Ala | Ile | Lys | Lys | Tyr | Leu | Cys | 565 | 570 |     | 575 |
| Thr | Asp | Cys | Pro | Thr | Pro | Ser | Gln | Cys | Val | Val | Ala | Arg | Thr | Leu | Gly | 580 | 585 |     | 590 |
| Lys | Gln | Gln | Thr | Val | Met | Ala | Ile | Ala | Thr | Lys | Ile | Ala | Leu | Gln | Met | 595 | 600 |     | 605 |
| Asn | Cys | Lys | Met | Gly | Gly | Glu | Leu | Trp | Arg | Val | Asp | Ile | Pro | Leu | Lys | 610 | 615 | 620 |     |
| Leu | Val | Met | Ile | Val | Gly | Ile | Asp | Cys | Tyr | His | Asp | Met | Thr | Ala | Gly | 625 | 630 | 635 | 640 |
| Arg | Arg | Ser | Ile | Ala | Gly | Phe | Val | Ala | Ser | Ile | Asn | Glu | Gly | Met | Thr | 645 | 650 |     | 655 |
| Arg | Trp | Phe | Ser | Arg | Cys | Ile | Phe | Gln | Asp | Arg | Gly | Gln | Glu | Leu | Val | 660 | 665 |     | 670 |
| Asp | Gly | Leu | Lys | Val | Cys | Leu | Gln | Ala | Ala | Leu | Arg | Ala | Trp | Asn | Ser | 675 | 680 | 685 |     |
| Cys | Asn | Glu | Tyr | Met | Pro | Ser | Arg | Ile | Ile | Val | Tyr | Arg | Asp | Gly | Val | 690 | 695 | 700 |     |
| Gly | Asp | Gly | Gln | Leu | Lys | Thr | Leu | Val | Asn | Tyr | Glu | Val | Pro | Gln | Phe | 705 | 710 | 715 | 720 |
| Leu | Asp | Cys | Leu | Lys | Ser | Ile | Gly | Arg | Gly | Tyr | Asn | Pro | Arg | Xaa | Thr | 725 | 730 |     | 735 |
| Val | Ile | Val | Val | Lys | Lys | Arg | Val | Asn | Thr | Arg | Phe | Phe | Ala | Gln | Ser | 740 | 745 |     | 750 |
| Gly | Gly | Arg | Leu | Gln | Asn | Pro | Leu | Pro | Gly | Thr | Val | Ile | Asp | Val | Glu | 755 | 760 | 765 |     |
| Val | Thr | Arg | Pro | Glu | Trp | Tyr | Asp | Phe | Phe | Ile | Val | Ser | Gln | Ala | Val | 770 | 775 | 780 |     |
| Arg | Ser | Gly | Ser | Val | Ser | Pro | Thr | His | Tyr | Asn | Val | Ile | Tyr | Asp | Asn | 785 | 790 | 795 | 800 |
| Ser | Gly | Leu | Lys | Pro | Asp | His | Ile | Gln | Arg | Leu | Thr | Tyr | Lys | Leu | Cys | 805 | 810 |     | 815 |
| His | Ile | Tyr | Tyr | Asn | Trp | Pro | Gly | Val | Ile | Arg | Val | Pro | Ala | Pro | Cys | 820 | 825 |     | 830 |
| Gln | Tyr | Ala | His | Lys | Leu | Ala | Phe | Leu | Val | Gly | Gln | Ser | Ile | His | Arg | 835 | 840 |     | 845 |
| Glu | Pro | Asn | Leu | Ser | Leu | Ser | Asn | Arg | Leu | Tyr | Tyr | Leu |     |     |     | 850 | 855 | 860 |     |

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<210> 8  
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Oligonucleotide Primer

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Oligonucleotide Primer

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<210> 12  
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 Oligonucleotide Primer  
  
 <400> 12  
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 <400> 15  
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 <400> 16  
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 <210> 17

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Oligonucleotide Primer

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23

<210> 18  
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Oligonucleotide Primer

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24

<210> 19  
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Oligonucleotide Primer

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24

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20

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